REMARKS

Claims 1, 34, 37, 40, and 43-45 have been amended. Claims 2-33, 35-36, 38-39 and 41-42 have been canceled without prejudice. Subsequent to the entry of the present amendment, claims 1, 34, 37, 40 and 43-47 are pending and at issue. These amendments and additions add no new matter as the claim language is fully supported by the specification and original claims.

Applicant acknowledges that the Terminal Disclaimer filed October 19, 2006 has been accepted and recorded.

I. Amendment to the Claims

Claims 1, 34, 37, 40 and 43 have been amended to recite those GDF-8 sequences which are fully supported in the parent application, U.S. Ser. No. 09/124,180, which was filed February 18, 1999, which priority date is enjoyed by the present application (discussed in more detail below). Claims 44 and 45 have been amended to replace "said" with the article --the--.

No new matter has been added.

II. Objection

Claim 40 is objected to as allegedly missing the closing parenthesis following "SEQ ID NO:18." The claim has been amended such that the sequence identifier has been removed, therefore the objection is moot. For this reason, Applicants respectfully request that the objection be withdrawn.

III. Rejections under 35 U.S.C. §102

Claims 1, 34, 37, 40, 43, 46 and 47 are rejected under 35 U.S.C. §102(e) as being allegedly anticipated by Barker et al. (U.S. Patent Number 6,369,201). Applicant respectfully traverses the rejection as it applies to the pending claims.

To anticipate, a single reference must inherently or expressly teach *each and every* element of claimed invention. *In re Spada*, 15 USPQ2d 1655 (Fed Cir. 1990); and *Verdegaal*

Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). MPEP § 2131. Further, the claimed invention must be distinct from what is apparently inherent in the reference, and the reference must be enabling to place the allegedly disclosed matter in the possession of the public. *In re Fitzgerald et al.*, 619 F.2d 67, 205 USPQ 594 (CCPA 1980); and *Akzo N.V. v. U.S. Int'l Trade Comm'n*, 1 USPQ2d 1241, 1245 (Fed. Cir. 1986).

The Office Action alleges, in pertinent part, that the cited reference is available as prior art because the elements as recited in the present claims (e.g. amino acids 1-20, 20 to 262 or 263, 267 or 268 to 374 of SEQ ID NOs:2, 4, 6, 8, 10. 12. 14, 16, 18 or 20) do not enjoy the priority date of U.S. Ser. No. 09/124,180, which was filed February 18, 1998 (hereinafter, the '180 application). Hence, Barker et al., filed on February 18, 1999, antedates the present application, which was filed on July 27, 2000.

Applicants submit that the claimed elements (GDF-8 sequences) are entitled to the priority date of the '180 application, i.e., July 28, 1998. The present claims recite "amino acid residues from about 1-20 of full length promyostatin (claim 1)"; "amino acid residues from about 20 to 262 or 263 of full length promyostatin (claim 34)"; "amino acid residues from about 20 to 262 of full length promyostatin (claim 37)"; "amino acid residues from about 267 or 268 to 374 or 375 of full length promyostatin (claim 40)"; "amino acid residues from about 267 to 374 of full length promyostatin (claim 43)"; "amino acid residues from about 20 to 263 of full length promyostatin (claim 46)"; and "amino acid residues from about 268 to 375 of full length promyostatin (claim 47)".

First, with regard to claims directed to "amino acid residues from about 1-20 of full length promyostatin", explicit support for this element can be found in Figures 6A and 6B of the '180 application, which describes that both murine and human GDF-8 homologs have the same hydrophobicity profile and contain "a core of hydrophobic amino acids at the N-terminus suggestive of a signal peptide for secretion." of the signal peptide. Similarly, the "Brief Description of the Drawings" states that:

> FIGURE 6 shows a hydropathicity profile of GDF-8. Average hydrophobicity values for murine (FIGURE 6a) and human (FIGURE 6b) GDF-8 were calculated using the method of Kyte and Doolittle (*J. Mol. Biol.*, 157:105-132, 1982). Positive numbers indicate increasing hydrophobicity.

Still, the last paragraph of Example 3 describes that:

> The predicted pre-pro-GDF-8 protein is 375 amino acids in length. *The sequence contains a core of hydrophobic amino acids at the N-terminus suggestive of a signal peptide for secretion* (FIGURE 6b)..

Thus, the '180 application clearly describes the signal peptide of at least murine and human GDF-8.

Regarding claims reciting residues 20-262 or 263, and residues 266 or 267 to 374 or 375, support for these elements in the '180 application may be found in the last paragraph of Example 3, which describes that:

> ...a putative RX)(R proteolytic cleavage site at amino acids 263-266. FIGURE 7 shows a comparison of the predicted murine (top) and human (bottom) GDF-8 amino acid sequences. Numbers indicate amino acid position relative to the N-terminus. Identities between the two sequences are denoted by a vertical line. *Murine and human GDF-8 are approximately 94% identical in the predicted pro-regions and 100% identical following the predicted RXXR cleavage sites* (emphasis added).

The skilled artisan would understand that a cleavage site at amino acids 263-266 generates a promyostatin polypeptide that ends at about amino acid 262 or 263 and a C-terminal fragment that starts at about amino acids 266 or 267 to the end of the polypeptide at about amino acids 374 or 375.

Further, regarding the claims reciting "amino acid residues from about 267 or 268 to 374 or 375", Example 5 of the '180 application describes that this region of GDF-8 is the proper post-translationally modified product secreted from cells transfected with a murine GDF-8 cDNA clone. Also, Example 8 clearly shows that this fragment possesses muscle cell growth regulatory activity by demonstrating that when the C-terminal region comprising the above identified residues is deleted in GDF-8 knockout mice, homozygous mutant mice were 30%

larger. Moreover, the '180 application expressly states that the C-terminal region between the recited species shows absolute conservation. Thus, claimed C-terminal region spanning amino acids 267/268 to 374/375 of a full length promyostatin polypeptide is clearly supported in the '180 application specification.

Additionally, the above passages from the '180 application with regard to murine and human GDF-8 sequences apply to the other described GDF-8 polypeptides, including rat, chicken, baboon, bovine, porcine and ovine as follows.

Exhibit A (ClustalW alignment, http://www.ebi.ac.uk/cgi-bin/clustalw) is an amino acid sequence alignment using the claimed sequences, SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14 and 16, which corresponds to SEQ ID NOS: 12, 14, 19, 21, 23, 25, 27 and 29 of the '180 application. Exhibit B represents the input for the ClustalW analysis (SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14 and 16), and Exhibit C represents the score of each aligned sequence as compared to each other, which corresponds to the alignment as described in Exhibit A. Exhibits A and C demonstrate that the claimed sequences, which sequences are represented in the '180 application, are substantially identical to each other and to the murine (SEQ ID NO:4; "4" in Exhibit A & C) and human (SEQ ID NO:2; "2" in Exhibit A & C) sequences. This type of analysis can be performed by one of ordinary skill in the art, and which analysis was available to the skilled artisan at the time of the filing of the '180 application.

The sequences in Exhibit A are named Sequence 1 through 8, corresponding to SEQ ID NOs:2, 4, 6, 8, 10, 12, 14 and 16 of the claimed invention, which again corresponds to SEQ ID NOs: 12, 14, 19, 21, 23, 25, 27, and 29 of the '180 application. For example, Sequence 1 and 2 (SEQ ID NO:2 and 4; human:mouse) is 96% identical; Sequence 1 and 3 (SEQ ID NO:2 and 6; human:rat) is 94% identical; Sequence 1 and 4 (SEQ ID NO:2 and 8; human:chicken "gallus") is 91% identical; Sequence 1 and 5 (SEQ ID NO:2 and 10; human:baboon) is 99% identical; Sequence 1 and 6 (SEQ ID NO:2 and 12; human:bovine) is 94% identical; Sequence 1 and 7 (SEQ ID NO:2 and 14; human:porcine) is 97% identical; and Sequence 1 and 8 (SEQ ID NO:2 and 16; human and ovine) is 94% identical. Substantially similar alignment scores are observed when the sequences are aligned with mouse, rat, chicken, baboon, bovine, porcine and ovine.

The average alignment score is 93.4% identity across the full-length of the GDF-8 sequence. Also, Exhibit A demonstrates that the cleavage site occurring at about amino acids 263-266, "RSRRD", is 100% conserved, as well as the C-terminal domain/region after the cleavage site.

Thus, based on the foregoing, the claimed elements/sequences are supported in the '180 application and such support is enjoyed by all the disclosed GDF-8 sequences and not just for human and murine sequences. Therefore, the claimed invention enjoys the benefit of priority of the '180 application, and the effective date for the instant amended claims *is* July 28, 1998. Because Barker et al. was filed on February 18, 1999, the reference is not available as prior art.

Accordingly, withdrawal of the rejection of the claims 1, 34, 37, 40, 43, 46 and 47 under 35 U.S.C. § 102(e) is respectfully requested.

Conclusion

In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to this application.

A check in the amount of $225.00 is enclosed to cover a Two-Month Petition for Extension of Time fee. The Commissioner is hereby authorized to charge any additional fees required by this submission, or make any credits or overpayments, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A copy of the Transmittal Sheet is enclosed.

Respectfully submitted,

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